REMARKS/ARGUMENTS

An Information Disclosure Statement was filed July 23, 2008 with PTO late fee. Consideration thereof is requested.

Claims 9-14 are rejected under 35 USC 112 on the reasoning that they are broader than enabled. More specifically, the Examiner considers that they are not enabled for other then squamous carcinomas.

Applicants respectfully disagree.

Example 1 of the present specification shows that a combined treatment of irradiation and administration of a compound of the formula (1) recited in Claim 1 (to be called as "combined treatment of the present invention", hereinafter) is effective for both of squamous carcinoma and adenocarcinoma. (See the present specification, page 16, line 16 to page 29, line 22.) More specifically, Experimental Examples 1-1 to 1-4 demonstrate that the combined treatment of the present invention is effective for tongue squamous carcinoma (SAS cells) derived from squamous carcinoma; Experimental Example 1-5 demonstrates that the combined treatment of the present invention is effective for esophageal cancer (TE-8 cells) derived from squamous carcinoma;

Experimental Example 1-6 demonstrates that the combined treatment of the present invention is effective for uterine cervical cancer (HeLa cells) derived from adenocarcinoma; and Experimental Example 1-7 demonstrates that the combined treatment of the present invention is effective for lung cancer (A549 cells) derived from adenocarcinoma.

We attach hereto a copy of a document which indicates that tongue squamous carcinoma (SAS cells) are derived from squamous carcinoma as "Exhibit 1"; a copy of a document which indicates that esophageal cancer (TE-8 cells) are derived from squamous carcinoma as "Exhibit 2"; copies of documents which indicate that uterine cervical cancer (HeLa cells) are derived from adenocarcinoma as "Exhibit 3" and "Exhibit 4"; and a copy of a document which indicates that lung cancer (A549 cells) are derived from adenocarcinoma as "Exhibit 5".

In addition, annexed is a Declaration which shows that the combined treatment of the present invention is also effective for other types of cancer, i.e., prostate adenocarcinoma (DU145 cells) derived from adenocarcinoma and colorectal adenocarcinoma (SW480 cells) derived from adenocarcinoma. (See Experiments 1 and 2 of the Declaration.)

There is also enclosed herewith a copy of a document which indicates that prostate adenocarcinoma (DU145 cells) are derived from adenocarcinoma as "Exhibit 6", and a copy of a document which indicates that colorectal adenocarcinoma (SW480 cells) are derived from adenocarcinoma as "Exhibit 7".

The descriptions of the Example 1 provided in the present specification and the contents of the Declaration clearly show that the combined treatment of the present invention is effective also for cancers other than squamous carcinoma.

Withdrawal of the formal objection is therefore requested.

There is also an art rejection of Claims 9-16 over Yamazaki et al with Hainfeld et al and Park et al.

Yamazaki et al. is cited for disclosing that the compound recited in Claim 10 of the present application (sulfoquinovosylacylglycerol derivative) has an effect as an anticancer agent, immunosuppressive agent and DNA polymerase a inhibitor. However Yamazaki et al. does not disclose or suggest the use of the compound as a radiosensitizer or any reason to expect a synergistic effect when it is so used.

Hainfeld et al. discloses carboplatin, cisplatin and oxaliplatin as a radiosensitizer, and Park et al. discloses N'-

(phenyl-pyridin-2-yl-methylene)-hydrazine carbodithioic acid methyl ester as a radiosensitizer. However, the radiosensitizers disclosed in Hainfeld et al. and Park et al. do not include a "sugar skeleton" or "acyl residue of higher fatty acid" of the compound of the formula (1) recited in Claim 1 of the present application (to be called as a "radiosensitizer of the present invention", hereinafter) and thus they have structures entirely different from that of the radiosensitizer of the present invention. Further, neither Hainfeld et al. nor Park et al. includes a description which suggests the chemical structure of the radiosensitizer of the present invention. It is therefore submitted that there is no reason in the art to conclude that compounds such as the compounds required by the present invention would have an effect as a radiosensitizer.

Furthermore, a synergistic effect is obtained by the combined treatment of the present invention. This is totally unexpected based on the prior art.

As can be seen from the illustrations of FIGS. 1 to 7 of the present application and the results of Experiments 1 and 2 described in the enclosed Declaration, when the radiosensitizer (used in the combined treatment of the present invention) is used

solely at the same concentration as the case of the combined treatment, it does not substantially exhibit an effect of suppressing the growth of cancer cells. (See -▲- in FIGS. 1 to 7; -■- in the Declaration, Experiment 1; and -•- in the Declaration, Experiment 2.) On the other hand, the combined treatment of the present invention (see -⊙- in FIGS. 1 to 7; -□- in the Declaration, Experiment 1; and -O- in the Declaration, Experiment 2) significantly suppresses the growth of cancer cells as compared to the case where the radiation is solely used (see -•- in FIGS. 1 to 7; and -▲- in the Declaration, Experiments 1 and 2). Thus, the effect on the growth suppression of cancer cells, which is obtained by the combined treatment of the present invention, is a totally unexpected synergistic effect, and such a synergistic effect.

From the results shown in FIGS. 8 to 19 of the present application, it can be understood that when the combined treatment of the present invention is used to suppress the proliferation of vascular endothelial cells, the value of the surviving fraction (SF value) of the vascular endothelial cells is remarkably lower than the theoretical additive point of the combined use, and thus the effect of suppressing the proliferation

of vascular endothelial cells is remarkably higher than the theoretical value. Thus, the effect on the proliferation suppression of vascular endothelial cells, which is obtained by the combined treatment of the present invention, is a synergistic effect, and such a synergistic effect cannot be expected by a person skilled in the art.

From the results shown in FIG. 20 of the present application, it can be understood that the combined treatment of the present invention ("Radiation + SQMG" in FIG. 20) exhibits a significantly high angiogenesis-suppressing effect as compared to the case where radiation is combined with a known radiosensitizer, Suramin ("Radiation + Suramin" in FIG. 20). Thus, the effect on the angiogenesis suppression, which is obtained by the combined treatment of the present invention, is a synergistic effect, and such a synergistic effect cannot be expected by a person skilled in the art.

In the combined treatment of the present invention, the radiosensitizer of the present invention exhibits its effect at a low administration concentration

It has been reported that when the radiosensitizer of the present invention (i.e., the compound of the formula (1) recited

in Claim 1 of the present application) is used solely, it has an anticancer activity (See Yamazaki et al.). In Example 1 of the present specification, the radiosensitizer of the present invention was administered 1 to 10 times at a concentration of 1 mg/kg (a total of 1 to 10 mg/kg) solely or in combination with irradiation. The results are shown in FIGS. 1 to 7 provided in the specification. In FIGS. 1 to 7, when the radiosensitizer of the present invention was administered solely at the above-mentioned concentration, the radiosensitizer does not at all or substantially exhibit its anti-cancer activity due to its low concentration, as in the case of the anticancer activity of the control. (See -▲- in FIGS. 1 to 7.) In other words, the radiosensitizer of the present invention can exhibit the radiosensitizing effect even at such a low concentration that it does not at all or substantially exhibit its anti-cancer activity. Such radiosensitizing effect can be regarded as "a synergistic effect" of the radiosensitizer administration and irradiation.

On the other hand, the radiosensitizer disclosed in Park et al. exhibits, as indicated in FIG. 5, an anti-cancer activity also when it is administered solely, and therefore the effect of

"combination (-◆-)" shown in FIG. 5 of Park et al. can be regarded as "an additive effect" of the radiosensitizer administration and irradiation.

Therefore, it is submitted that it cannot be expected by a person skilled in the art that the radiosensitizer of the present invention can exhibit the radiosensitizing and that the effect is available even at such a low concentration that it does not at all or substantially exhibit its inherent anti-cancer activity. A lower concentration of the radiosensitizer in administration leads to a solution to the problem of side effect.

A further surprising advantage is that the radiosensitizer of the present invention exhibits the therapeutic effect even when it is used in combination with a low dose of irradiation.

Experiment 3 provided in the Declaration shows that the radiosensitizer of the present invention is effective as a radiosensitizer when it is used in combination with 2 times of irradiation at a dose of 2 Gy.

As presented in Experiment 3 of the Declaration, the combined treatment of irradiation at a dose of 2 Gy (a total of 4 Gy) and administration of the radiosensitizer (indicated by -▲- in the graph) exhibits an anti-tumor effect as high as that of

the cases of solely irradiation at a dose of 6 Gy (a total of 12 Gy) (indicated by -■- in the graph) and the combined treatment of irradiation at a dose of 6 Gy (a total of 12 Gvl and administration of the radiosensitizer (indicated by -□- in the graph). On the other hand, Park et al. describes, in Example 3 on page 5, a combined treatment of 5 times of irradiation at a dose of 5 Gy (a total of 25 Gy) and administration of a compound. Thus, the combined treatment of the present invention can exhibit a high anti-tumor effect even in the case of a low dose of irradiation. Therefore, the combined treatment of the present invention can reduce the radiation dose and thereby reduce the side effects caused by irradiation on a patient to be treated.

As discussed in the response to the rejection under 35 USC 112, paragraph 1, it has been demonstrated that the combined treatment of the present invention exhibits its advantageous effect against various types of cancers. On the other hand, Park et al. discloses that "radiotherapy has been reported to be effective in treating only specific kinds of cancers such as lung cancer, mammary cancer, and uterine cancer, while some other kinds of cancers show only partial effects or develop resistance to radiotherapy". (See the outstanding official Action, page 4,

lines 6 to 9.) Despite such disclosure of Park et al., it has been demonstrated by the present invention that the combined treatment of the present invention exhibits its advantageous effect against various types of cancers. Thus, the effectiveness of the present invention against various types of cancers cannot be expected by a person skilled in the art.

In view of the above, the rejections are avoided. Allowance of the application is therefore respectfully requested.

Respectfully submitted,

Frishauf, Holtz, Goodman
& Chick, P.C.
220 Fifth Ave., 16th Floor
New York, NY 10001-7708
Tel. No.: (212) 319-4900
Fax No.: (212) 319-5101
MJC:sg

MARSHALL J. CHICK
Reg. No. 26,853

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